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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/687,609	10/13/2000	Roberto Weinmann	BMS-0010	9813

7590 11/05/2002
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EXAMINER

CLOW, LORI A

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 11/05/2002

9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/687,609

Applicant(s)

WEINMANN ET AL.

Examiner

Lori A. Clow, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 August 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14, 18 and 19 is/are pending in the application.
- 4a) Of the above claim(s) 15-17 and 20-32 is/are withdrawn from consideration.
- 5) ☒ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-14, 18, and 19 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4. 6) ☐ Other: _____

DETAILED ACTION

Applicant's election with traverse of Group I, claims 1-14, 18, and 19, in Paper No.8, filed 2 August 2002, is acknowledged. The traversal is on the grounds that the inventions as claimed can be readily evaluated in one search without placing an undue burden on the Examiner. Applicant's argument is not found persuasive for the reasons set forth in the Restriction/Election Requirement in Paper No. 7, mailed June 2002. In the requirement, specific distinctions between the multiple inventions were set forth and as such the requirement is still deemed proper and is made FINAL.

Applicant's arguments regarding the Election of Species have been found persuasive and this requirement has been withdrawn.

Claims 1-14, 18, and 19 are currently pending. Claims 15-17, and 20-32 have been withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or

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absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

Claims 1-14, 18 and 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a crystal of an AR-LBD complex, does not reasonably provide enablement for an AR-LBD or an AR-LBD ligand, separately. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The table referred to in the specification is Table A. As defined in the specification at page 5, lines 22-30, the coordinates pertain to the androgen receptor and **not** to the complex of androgen receptor plus ligand. The three-dimensional structure of this complex of receptor plus ligand is contemplated, however, the coordinates of what is actually contained in the physical crystal reflect the receptor itself. Thus, the specification does enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Furthermore, in the field of protein crystallography, it is well established that the utilization of a variety of crystallization methods, for the protein in question, greatly improves the chances of identifying suitable conditions for crystallization. It is well known that the homologous proteins from different sources cannot be easily crystallized using the same technique and/or conditions and may result in different crystal forms. See, for example, Jan Drenth ("Principles of Protein X-ray Crystallography" (1994), Springer-Verlag, New York, pages 1-9).

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While the skill in the art of crystallography is high, the science of protein structure and obtaining crystals is still uncertain. The slightest variations in the way of receiving protein structure information and measurement could cause failure in obtaining useful results. Although working examples, per se, are not required, the specification must provide an enabling disclosure for the invention without undue experimentation. It is noted that only the crystal that is defined by Table A, the androgen receptor and its ligand binding domain (AR-LBD), is enabled in the specification and it would require undue experimentation to determine the crystal structure of homologues, mutants, and complexes, for the reasons noted above.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11-14 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims refer to "molecular complex" and this could potentially have two definitions. In the specification "complex" refers to the complex of the AR-LBD plus its ligand, but also refers to a "complex" as the AR and its LBD. The examiner has interpreted "complex" as the former. Also, does molecular complex refer to a protein or a set of coordinates?

Claim 13 recites a complex "comprising all or any part of the ligand binding site." Does this mean that a single amino acid would apply?

Claims 18 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear as to what is meant by "binding site." As read, binding

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site could refer to a protein binding site, a three-dimensional model of the binding site, or a set of coordinates of the binding site. Further the claims are drawn to a binding site with no specifically recited ligand. Therefore it would not be possible to be in contact with the recited residues of the site.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 11-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Kuil et al. (The Journal of Biological Chemistry (1995) Vol.17, pages 27569-27576). Claims 11-14 do not require crystals, therefore, Kuil et al. anticipate said molecule or molecular complex by disclosing produced androgen receptor complexes that would inherently contain said amino acids if binding sites are conserved (see materials and methods, p. 27570). Furthermore, these complexes could also be deemed mutants and/or homologs if the binding sites are not conserved.

Prior Art

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

A. Koutsilieris, M. *et al.* J. of Androl. (1990) Vol. 11, No. 1, pages 2-8.

B. Radwan *et al.* J. Steroid Biochem. (1988) Vol. 30, No. 1-6, pages 251-255.

C. Nakahara, M. Hinyokika Kyo (1986) Vol. 32, No. 11, pages 1689-1699.

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D. Chang *et al.* Biochemistry (1982) Vol. 21, No.17, pages 4102-4109.

E. Foekens *et al.* Mol. Cell Endocrinol. (1981) Vol. 23, No. 2, pages 173-186.

No claims are allowed.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242, or (703) 308-4028.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (703) 306-5439. The examiner can normally be reached on Monday-Friday from 10am to 6:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Patent Analyst, Bill Phillips, whose telephone number is (703) 305-3419, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

Marianne P. Allen
MARIANNE P. ALLEN
PRIMARY EXAMINER
GROUP 1631
A11631

November 4, 2002

Lori A. Clow, Ph.D.

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Lori A. Clow